

Figure 1

- A. ctc aac cag tcc att gtc ca
B. tcc egg ttg ctc tga gac at
C. gcc aca gtc atg ccc gtc ag
D. ctg cga tcc gac tca cca at
E. agt cct gtt ctc ttc cac
F. ctt tac tgc tgc cat ggg
G. cgc cgt tct cct gga tcc aa
H. ctg act cca gct gta tcc
I. ggt ctc cat ctc cga ttc
J. cct ggg gtg atg tgg agc
K. agt tcc aca aaa gta tcc
L. ctt tcg gct ctc ggc tgc
M. aac cag cgg ttg aag cgt

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Figure 2A

- A. (T31028)
c*t*c* aac* cag t*c*c at*t gt*c* c*a
- A'. (T31029)
C*T*C* aaC* Cag T*C*C aT*T gT*C* C*a
- B. (T31030)
t*c*c* cgg t*tg c*t*c* tga ga*c* a*t
- C. (T31044)
g*c*c* aca gt*c atg c*c*c gt*c* a*g
- C'. (T31045)
g*C*C* aCa gT*C aTg C*C*C gT*C* a*g
- D. (T31049)
CT*g Cga T*C*C gaC* T*Ca C*C*a* a*t
- E. (T31054)
a*g*t* c*c*t gt*t c*t*c t*t*c* c*a*c
- E'. (T31055)
a*g*T* C*C*C* g*T*T C*T*C T*T*C* C*a*c
- F. (T31061)
C*T*T* TaC TgC* TgC* CaT* g*g*g
- G. (T31043)
C*gc* C*gT* T*C*T* C*C*T gga TC*C* a*a
- G'. (T31042)
c*gc* c*gt* t*c*t* c*c*t gga tc*c* a*

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Figure 2B

H. (T31053)
C*T*G* aC*T* C*Ca gC*T gTa* T*C*c

H'. (T31052)
c*t*g* ac*t* c*ca gc*t gta* t*c*c

I. (T31057)
g*g*T* CT*C* CaT* CT*C Cga* T*T*c

I'. (T31056)
g*g*t* ct*c* cat* ct*c cga* t*t*c

J. (T31062/63)
c*c*t* ggg gtg* atg* tgg* a*g*c

K. (T31065)
a*g*T* TC*C aC*a aaa gT*a* T*C*c

K'. (T31064)
a*g*t* tc*c ac*a aaa gT*a* t*c*c

L. (T31067)
C*T*T* Tcg gC*T C*T*C ggC* T*g*c

L'. (T31066)
c*t*t* tcg gc*t c*t*c ggc* t*g*c

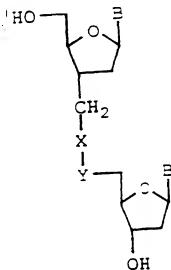
M. (T31069)
a*a*C* Cag Cgg T*Tg aag* C*g*t

M'. (T31068)
a*a*c* cag cgg t*t*g aag* c*g*t

where * = phosphorothioate
C = Propynyl dC
T = Propynyl dT

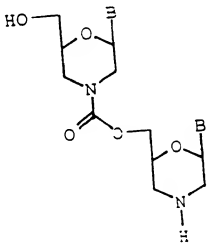
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Figure 3A



Hydroxylamine
MOMI
MMI

X	Y
N-H	O
O	N-CH ₃
N-CH ₃	O

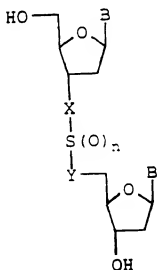


Morpholino-carbamate

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Figure 3B



n = 2
 Sulfate
 Sulfonate
 Sulfone
 Sulfamate
 Sulfonamide

X
 O
 O
 CH,
 O
 NH

Y
 O
 CH,
 CH,
 NH
 CH,

n = 1
 Sulfite
 Sulfoxide

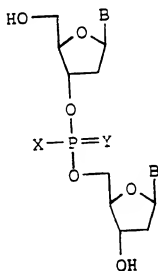
O
 CH,

O
 CH,

n = 0
 Sulfide

CH,

CH,



Phosphodiester
 Phosphorothioate
 Phosphorodithioate
 Methylphosphonate
 Phosphotriester
 Phosphoramidate
 Boranophosphate

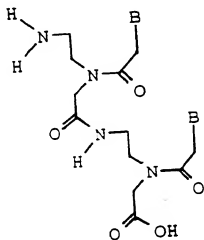
X
 O-
 S-
 S-
 CH,
 O-R
 NH-R
 BH,

Y
 O
 O
 S
 O
 O
 O
 O

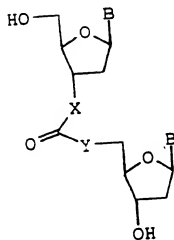
00753159 010201

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Figure 3C



PNA dimer



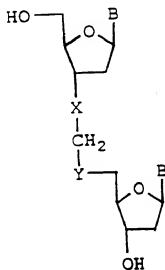
Carbonate
5'-N-carbamate

X
O
O

Y
O
NH

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Figure 3D



Formacetal
5' - Thioether
3' - Thioformacetal
5' - Thioformacetal

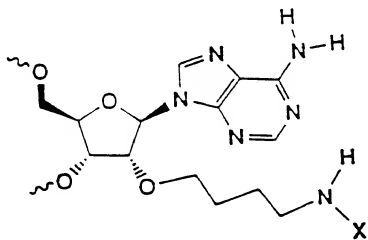
$$\begin{array}{c} \text{X} \\ | \\ \text{O} \\ | \\ \text{CH}_2 \\ | \\ \text{S} \\ | \\ \text{O} \end{array}$$

Y
O
S
O
S

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Figure 4

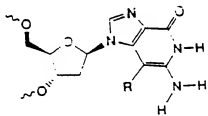


X = BIOTIN
= CHOLIC ACID
= FLUORESCIEIN

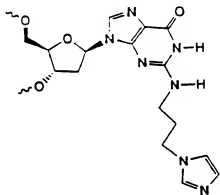
2'-O-(AMINOPENTYL) ADENINE
CONJUGATES

900-876-2222

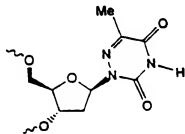
Figure 5A



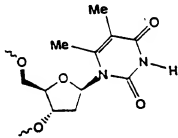
3-DEAZAGUANINES



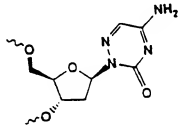
N2-IMIDAZOLYLPROPYL
GUANINE



6-AZATHYMIDINE



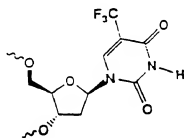
5,6-DIMETHYLTHYMIDINE



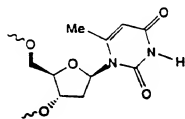
6-AZA-DEOXYCYTIDINE

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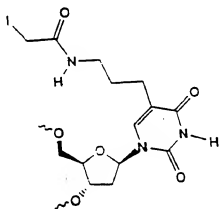
Figure 5B



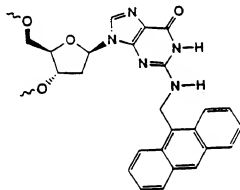
TRIFLUOROTHYMININE



6-METHYLTHYMININE



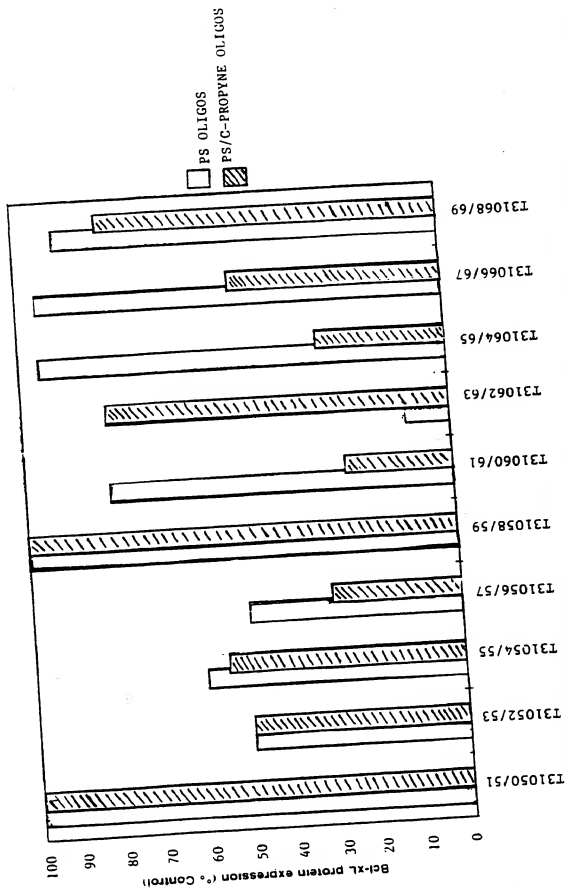
IDOACETAMIDOPROPYL URACIL



N2-ANTRACENYLMETHYL
GUANINE

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FIGURE 6 Effect of 18-mer PS oligonucleotides on bcl-xL protein expression in LNCap cells



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FIGURE 7

LNCaP cell line

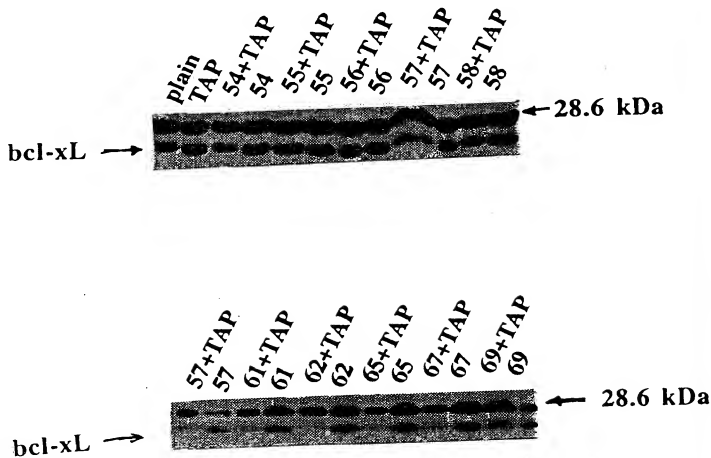


FIG. 8
Antisense Oligonucleotides to Bcl-xL mRNA

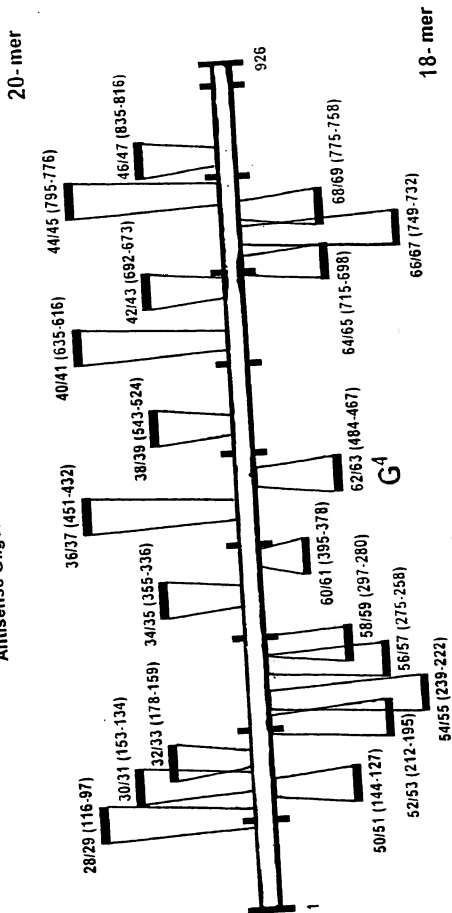
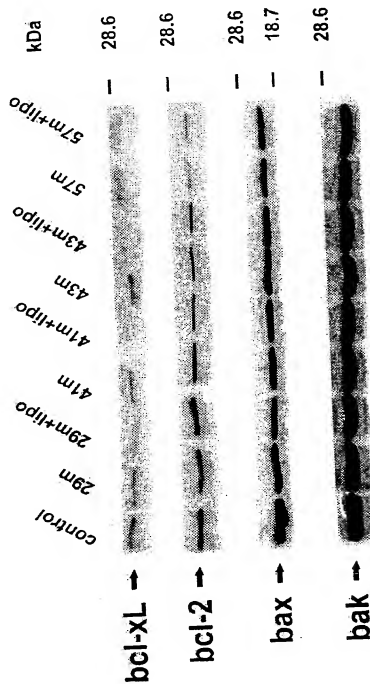


FIG. 9

Regulation of Bcl-Family Proteins with 2'-O-Methyl - Modified PS Oligonucleotides in T24 Cell Line



Delivery: 1 uM oligo, 5 ug/ml Lipofectin

FIG. 10

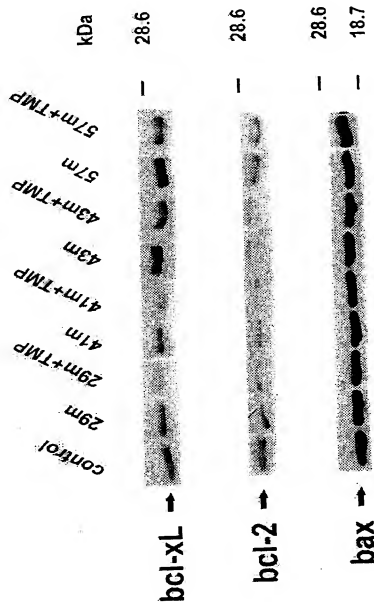
The Most Active Chimeric PS-PO Oligonucleotides by
Their Ability to Down-Regulate Bcl-xL Protein Expression

5'-
29 C*T*C*a a C* C a g T*C* C a T*T g T*C* C*a
41 C T*g* C g a T*C* C g a C* T* C a C*C*a* a*t
43 C*g C* C*g T* T*C*T* C*C*T g g a T C*C*a*a
57 g*g*T* C T*C* C a T* C T*C C g a T*T*c
61 C*T*T* T a C T g C* T g C* C a T* g*g*g
62 c*c*t* g g g g t g* a t g* t g g* a*g*c
63 C*C*T* g g g g T g* a T g* t g g* a*g*
C, T - propynyl modified bases, * - PS

-3'

FIG. 11

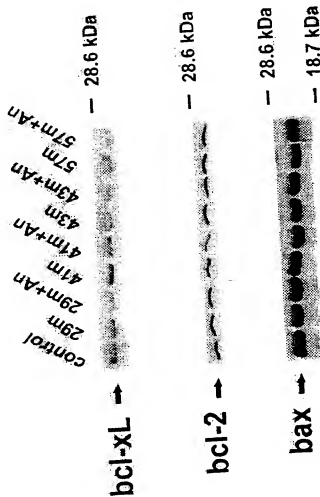
Regulation of Bcl-Family Proteins with 2'-O-Methyl - Modified PS Oligonucleotides in PC - 3 Cell Line



Delivery: 1uM oligo, 5 uM TMP

FIG. 12

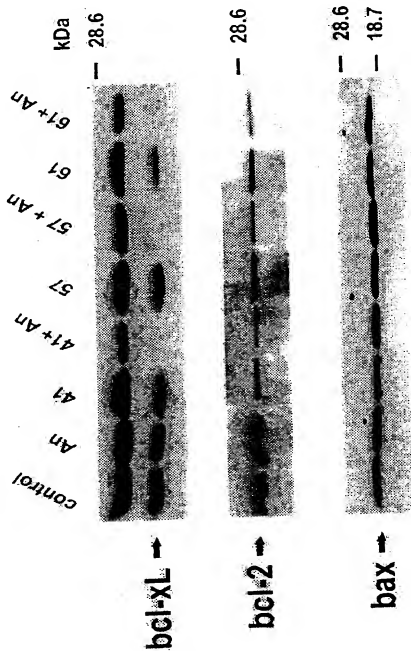
Regulation of Bcl-xL and Bax Proteins with 2'-O-Methyl-Modified PS Oligonucleotides in LNCaP Cell Line



Delivery: 1 uM oligo, 5 uM An

FIG. 13

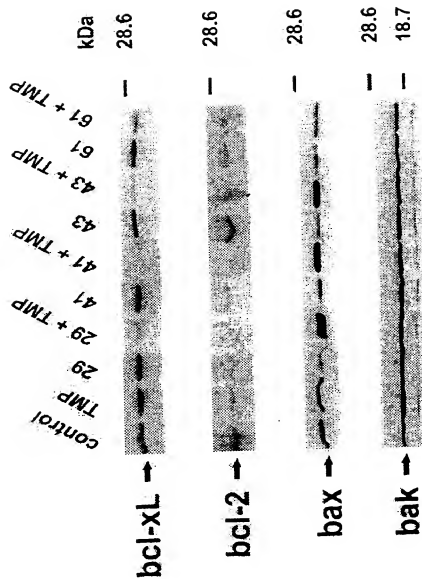
Down-Regulation of Bcl-Family Proteins Expression with PS-PO Oligonucleotides in LNCaP Cell Line



Delivery: 1uM oligo, 3 uM An

FIG. 14

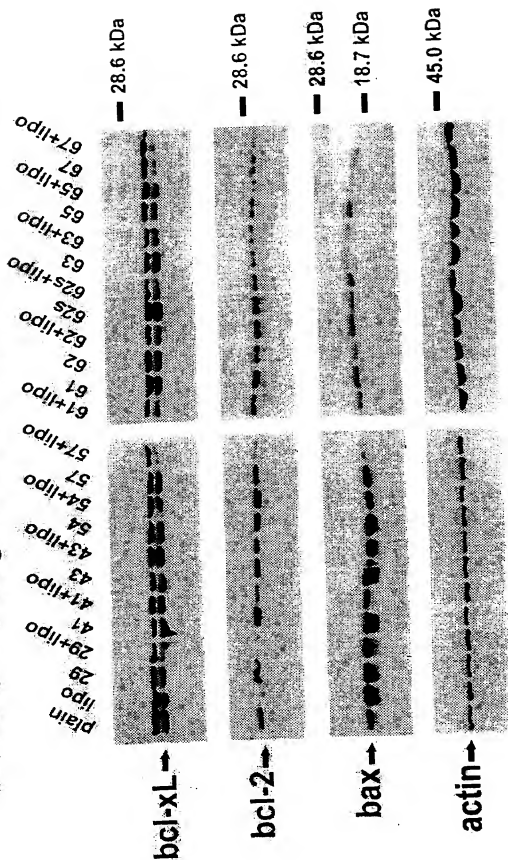
Down-Regulation of Bcl-Family Proteins Expression with PS-PO Oligonucleotides in PC3 Cell Line



Delivery: 2 uM oligo, 7 uM TMP

FIG. 15

Regulation of Bcl-Family Proteins with PS-PO Oligonucleotides in T24 Cell Line



Delivery: 0.5 μ M oligo, 5 mg/ml lipofectin

FIG. 16

Down-Regulation of Bcl-xL mRNA with PS-PO Oligonucleotides in T24 Cell Line

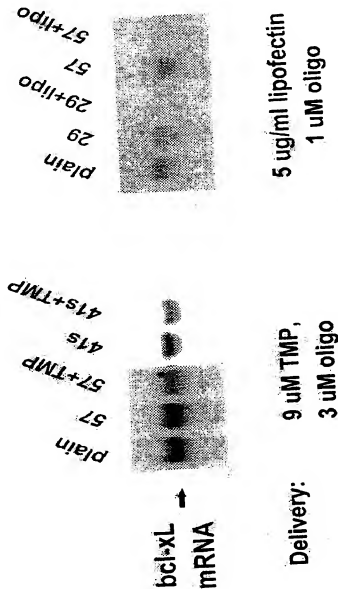
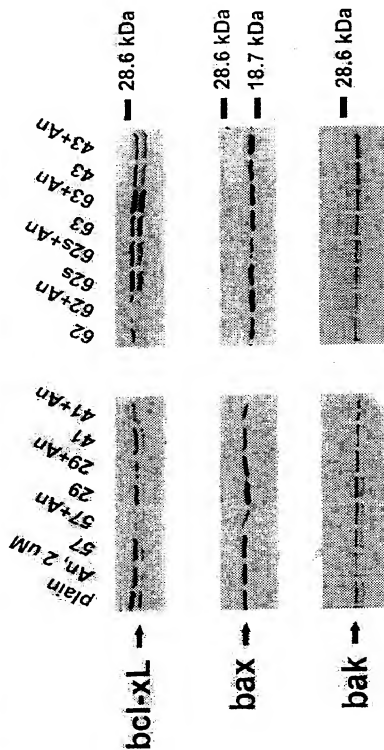


FIG. 17

Regulation of Bcl-Family Proteins with PS-PO Oligonucleotides in LNCaP Cell Line



Delivery: 1 uM oligo, 3 uM An